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Office of Surveillance and Epidemiology

Drug Use Review

Date:	October 19, 2011
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Drug Name(s):	Xerese® (acyclovir and hydrocortisone) cream
Application Type/Number:	NDA 22-436
Applicant/sponsor:	Medivir AB/Contract Pharmaceuticals Limited
OSE RCM #:	2011-1401

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CONTENTS

EXECUTIVE SUMMARY

This review examines drug utilization patterns in the pediatric population (0-16 years) for Xerese® (5% acyclovir combined with 1% hydrocortisone) cream from November 1, 2010 through August 31, 2011. Since the majority of this product was sold to U.S. outpatient retail pharmacy settings (96% of Xerese® tubes distributed to outpatient retail pharmacies), this review focuses on outpatient utilization patterns. Although Xerese® was approved on July 31, 2009, data were not captured until November 1, 2010, due to the delayed market launch of this product.

U.S. Outpatient retail pharmacy data summary from November 1, 2010 through August 31, 2011, cumulative:

- Approximately 6,100 prescriptions were dispensed and 5,300 patients received a dispensed prescription for Xerese® from U.S. outpatient retail pharmacies from November 1, 2010 through August 31, 2011, cumulative.
- Xerese® prescriptions dispensed to the pediatric population aged 0-16 years accounted for approximately 5% of prescriptions (300 prescriptions) and 5% of patients (265 patients).
- General Practice/Family Medicine was the top prescribing specialty accounting for 23% of Xerese® prescriptions, while Pediatricians accounted for less than 1% of Xerese® prescriptions.
- Diagnosis mentions associated with the use of Xerese® were not captured in pediatric patients aged 0-16 years. The only diagnosis associated with the use of Xerese® for patients aged 17 years and older was "Herpes simplex NOS".

1 BACKGROUND

1.1 INTRODUCTION

In preparation for the upcoming Pediatric Advisory Committee meeting in January 2012, the Division of Epidemiology (DEPI II) has been requested by the Office of Pediatric Therapeutics (OPT) and Pediatric and Maternal Health Staff (PMHS) to provide drug utilization data for Xerese® (acyclovir and hydrocortisone) cream. Specifically, we were asked to focus on drug utilization patterns in terms of the number of prescriptions and patients in the pediatric (ages 0-16 years) and adult (ages 17 years and older) populations, as well as prescriber specialties, and diagnoses associated with Xerese® use from the date of product approval on July 31, 2009 through August 31, 2011. However, Xerese® did not begin market launch until August 2010, and no drug utilization data were captured until November 2010, due to the delayed market launch of this product. Therefore, using the currently available proprietary drug use databases licensed by the Agency, this review describes outpatient retail pharmacy drug utilization patterns in the U.S. pediatric population for Xerese® from November 1, 2010 through August 31, 2011.

1.2 PRODUCT INFORMATION[1]

Xerese® (5% acyclovir and 1% hydrocortisone) cream is a topically administered combination product applied 5 times daily for 5 days. Xerese® was approved for the early treatment of recurrent herpes labialis (cold sores) to reduce the likelihood of ulcerative cold sores and to shorten the lesion healing time in adults and adolescents (12 years of age and older).

2 METHODS AND MATERIALS

2.1 DETERMINING SETTINGS OF CARE

IMS Health, IMS National Sales Perspectives™ Sales Perspectives (see ***Appendix 2*** for full database description) was used to determine the various retail and non-retail channels of distribution for Xerese® cream. Sales data for 12-month period ending June 2011 indicated that approximately 96% of Xerese® tubes (Eaches) were distributed to outpatient retail pharmacies; 3% to non-retail pharmacies; and 1% to mail order settings[2]. As a result, outpatient retail pharmacy utilization patterns were examined. Neither mail order nor non-retail settings data were included in this analysis.

2.2 DATA SOURCES USED

Proprietary drug use databases licensed by the Agency were used to conduct this analysis (see ***Appendix 2***).

Drug utilization data for Xerese® was searched from the date of product approval on July 31, 2009 through August 31, 2011. However, no drug utilization data were captured until November 2010, due to the delayed market launch of this product.

Therefore, U.S. outpatient utilization and patient demographics were obtained from SDI, Vector One®: National (VONA) and Total Patient Tracker (TPT) from November 1, 2010 through August 31, 2011, monthly and cumulative. From these two sources, nationally projected estimates of the prescriptions dispensed from retail pharmacies and the number of patients who received a dispensed prescription for Xerese® were stratified by the following patient age bands: 0-16 years, and 17 years or greater. The top prescribing specialty associated with the use of Xerese® was also obtained from SDI, Vector One®: National (VONA). Diagnoses associated with the use of Xerese® cream were obtained from SDI's, Physician Drug and Diagnosis Audit (PDDA) with Pain Panel, from November 1, 2010 through August 31, 2011.

3 RESULTS

3.1 PRESCRIPTIONS DISPENSED AND PATIENTS RECEIVING PRESCRIPTIONS FOR XERESE® BY PATIENT AGE

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[1] Xerese® [package insert]. Huddinge, Sweden. Manufactured by Contract Pharmaceuticals Limited, Mississauga, Ontario. May 2010

[2] IMS Health, IMS National Sales Perspectives™ Database. MAT June 2009-June 2011. Extracted August 2011. File: 1108tami.xls.

Table 1 (Appendix 1) shows the projected number of prescriptions dispensed and patients receiving dispensed prescriptions for Xerese® from U.S. outpatient retail pharmacies, stratified by patient age from November 1, 2010 through August 31, 2011. Approximately 6,100 prescriptions were dispensed for Xerese® during the examined time period. Xerese® prescriptions were primarily dispensed to adult patients aged 17 years and older at 95% (5,800 prescriptions) of the total. Around 5% (300 prescriptions) of Xerese® prescriptions were dispensed to pediatric patients aged 0-16 years. Approximately 5,300 patients received a prescription for Xerese® during the examined time period. Pediatric patients aged 0-16 years accounted for 5% of total patients (265 patients).

3.2 TREND OF PATIENTS WHO RECEIVED A PRESCRIPTION FOR XERESE® BY PATIENT AGE

Figure 1 (Appendix 1) graphically displays the monthly trends of the projected number of patients who received a dispensed prescription for Xerese® from U.S. outpatient retail pharmacies by patient age from November 1, 2010 through August 31, 2011. There has been a gradual increase in the number of patients receiving dispensed prescriptions for Xerese® since November 2010. Each month, more than 93% of patients receiving dispensed prescriptions for Xerese® were adults aged 17 years and greater.

3.3 XERESE® UTILIZATION BY PRESCRIBING SPECIALTY

Table 2 (Appendix 1) shows the top ten prescribing specialties for Xerese® by the projected number of prescriptions dispensed from U.S. outpatient retail pharmacies from November 1, 2010 through August 31, 2011, cumulative. During the examined time period "General Practice/Family Medicine/Doctor of Osteopathy" was the top prescribing specialty, accounting for approximately 23% (1,400 prescriptions) of total dispensed prescriptions. "Dermatology" accounted for 22% (1,300 prescriptions) of prescriptions, and "OB/GYN" accounted for 15% (882 prescriptions) of prescriptions. Prescriptions dispensed by the "Pediatric" specialty accounted for approximately less than 1% (46 prescriptions; data not shown) of total dispensed prescriptions for Xerese®.

3.4 DIAGNOSIS ASSOCIATED WITH THE USE OF XERESE®

The diagnoses associated with the use of Xerese® according to U.S. office-based physician practices was stratified by patient age from November 1, 2010 through August 31, 2011. Diagnoses were coded according to the International Classification of Diseases (ICD-9-CM). The only diagnosis captured during the study period for Xerese® was "Herpes simplex NOS" (ICD-9 code 054.9) in patients aged 17 years and older. The point estimate for the number of mentions associated with the diagnosis "Herpes simplex NOS" was 19,000 uses (95% CI, 0 – 40,000 uses). Pediatric use for patients aged 0-16 years was too low to be captured in this database.[3]

4 DISCUSSION

[3] SDI: Physicians Drug and Diagnosis Audit. Data extracted 9-30-11. File: PDDA 2011-1401 Xerese BPCA age 4ddx.xls

Findings from this review should be interpreted in the context of the known limitations of the databases used. We estimated that Xerese® products were distributed primarily to the outpatient retail pharmacy setting based on the IMS Health, IMS National Sales Perspectives™. Sales data do not provide a direct estimate of use but do provide a national estimate of units sold from the manufacturer into the various channels of distribution. The amount of product purchased by these channels of distribution may be a possible surrogate for use, if we assume the facilities purchase drugs in quantities reflective of actual patient use.

We focused our analysis on only the outpatient retail pharmacy; therefore these estimates may not apply to other settings of care in which these products are used (e.g. mail order). The estimates provided are national estimates from retail pharmacy dispensing for prescriptions and patient counts, but no statistical tests were performed to determine statistically significant changes over time. Therefore, all changes over time should be considered approximate, and may be due to random error.

Indications for use were obtained using SDI's PDDA, a monthly survey of 3,200 office based physicians. Although PDDA data are helpful to understand how drug products are prescribed by physicians, the small sample size and the relatively low usage of these products limits the ability to identify trends in the data. In general, PDDA data are best used to identify the typical uses for the products in clinical practice, and the VONA outpatient prescription data to evaluate trends over time. SDI recommends caution interpreting projected annual uses or mentions below 100,000 as the sample size is very small with correspondingly large confidence intervals. The point estimate for the number of mentions associated with the diagnosis "Herpes simplex NOS" was 19,000 uses with the true number of mentions falling in the range between 0 uses and 40,000 uses. However, the point estimate was below the count to provide a reliable national estimate of use for this diagnosis.

SDI uses the term "drug uses" to refer to mentions of a drug in association with a diagnosis during an office-based patient visit. This term may be duplicated by the number of diagnosis for which the drug is mentioned. It is important to note that a "drug use" does not necessarily result in prescription being generated. Rather, the term indicates that a given drug was mentioned during an office visit.

5 CONCLUSIONS

Xerese® is indicated for the early treatment of recurrent herpes labialis (cold sores) to reduce the likelihood of ulcerative cold sores and to shorten the lesion healing time in adults and adolescents (12 years of age and older). In the U.S. outpatient retail pharmacy setting, approximately 6,100 prescriptions were dispensed and 5,300 patients received a dispensed prescription for Xerese® for the cumulative time period November 1, 2010 through August 31, 2011. Outpatient prescriptions dispensed for Xerese® in the pediatric population aged 0-16 years accounted for approximately 5% of prescriptions dispensed (300 prescriptions) and 5% of patient counts (265 patients). General Practice/Family Medicine was the top prescribing specialty for Xerese® prescriptions and Pediatricians accounted for less than 1% of total dispensed prescriptions for Xerese®. Diagnosis mentions associated with the use of Xerese® were not captured in pediatric patients aged 0-16 years.

APPENDICES

APPENDIX 1: TABLES AND FIGURES

Table 1.

Projected number of dispensed prescriptions and patients receiving dispensed prescriptions for Xerese through U.S. outpatient retail pharmacies

	11/2010-08/2011			
	TRx	*Share %*	**Pts**	*Share %*
Xerese	**6,053**	*100.0%*	**5,336**	*100.0%*
0-16 yrs	**302**	*5.0%*	**265**	*5.0%*
17+ yrs	**5,751**	*95.0%*	**5,070**	*95.0%*

Source: SDI, Vector One®: National (VONA) and Total Patient Tracker (TPT). Extracted 9-21-11.

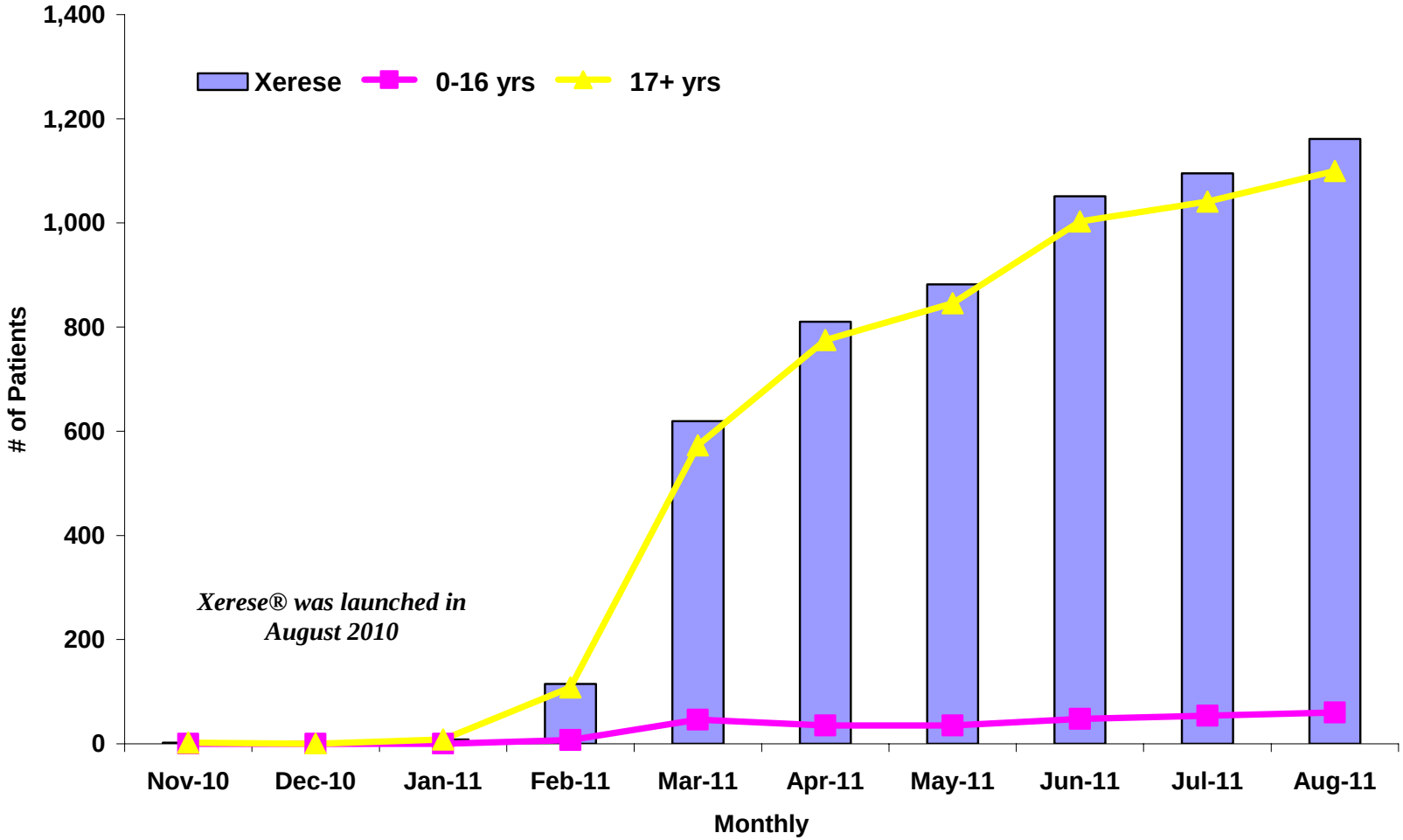
Files: VONA 2011-1401 Xerese BPCA ages 9-21-11.xls, TPT 2011-1401 Xerese BPCA age 9-21-11.xls

and TPT 2011-1401 Xerese BPCA age aggr 9-21-11.xls

Note: Xerese® was launched in August 2010

Figure 1.

Projected Number of Patients filling U.S. Retail Pharmacy Dispensed Xerese® Prescriptions, monthly November 1, 2010 through August 31, 2011



Source: SDI, Vector One®: Total Patient Tracker (TPT). Extracted 9-21-11.Files: TPT 2011-1401 Xerese BPCA age 9-21-11.xls and TPT 2011-1401 Xerese BPCA age aggr 9-21-11.xls

Table 2.

Projected Number of U.S. Retail Pharmacy Dispensed Xerese® Prescriptions by Top Ten Prescribing Specialties, cumulative November 1, 2010 through August 31, 2011

	11/2010-08/2011 TRxs	*11/2010-08/2011 Share% TRxs*
Xerese	**6,053**	*100.0%*
GP/FM/DO	**1,377**	*22.7%*
DERM	**1,345**	*22.2%*
OB/GYN	**882**	*14.6%*
IM	**569**	*9.4%*
NP	**416**	*6.9%*
UNSPEC	**393**	*6.5%*
PA	**343**	*5.7%*
ENT	**182**	*3.0%*
ALLER/IMMU	**121**	*2.0%*
EM	**91**	*1.5%*
Others	**337**	*5.3%*

Source: SDI, Vector One®: National (VONA). Extracted 9-21-11. File: VONA 2011-1401 Xerese BPCA specialty 9-21-11.xls

APPENDIX 2: DATABASE DESCRIPTIONS

IMS Health, IMS National Sales Perspectives™: Retail and Non-Retail

The IMS Health, IMS National Sales Perspectives™ measures the volume of drug products, both prescription and over-the-counter, and selected diagnostic products moving from manufacturers into various outlets within the retail and non-retail markets. Volume is expressed in terms of sales dollars, eaches, extended units, and share of market. These data are based on national projections. Outlets within the retail market include the following pharmacy settings: chain drug stores, independent drug stores, mass merchandisers, food stores, and mail service. Outlets within the non-retail market include clinics, non-federal hospitals, federal facilities, HMOs, long-term care facilities, home health care, and other miscellaneous settings.

SDI's Vector One®: National (VONA)

SDI's VONA measures retail dispensing of prescriptions or the frequency with which drugs move out of retail pharmacies into the hands of consumers via formal prescriptions. Information on the physician specialty, the patient's age and patient sex, and estimates for the numbers of patients that are continuing or new to therapy are available.

The Vector One® database integrates prescription activity from a sample received from payers, switches, and other software systems that may arbitrage prescriptions at various points in the sales cycle. Vector One® receives over 1.4 billion prescription claims per year, representing over 120 million unique patients. Since 2002 Vector One® has captured information on over 8 billion prescriptions representing over 200 million unique patients.

Prescriptions are captured from a sample from the universe of approximately 59,000 pharmacies throughout the U.S. The pharmacies in the database account for most retail pharmacies and represent nearly half of retail prescriptions dispensed nationwide. SDI receives all prescriptions from approximately one-third of stores and a significant sample of prescriptions from many of the remaining stores.

SDI's Vector One®: Total Patient Tracker (TPT)

SDI's Total Patient Tracker is a national-level projected audit designed to estimate the total number of unique patients across all drugs and therapeutic classes in the retail outpatient setting over time.

TPT derives its data from the Vector One® database which integrates prescription activity from a sample received from payers, switches, and other software systems that may arbitrage prescriptions at various points in the sales cycle. Vector One® receives over 1.4 billion prescription claims per year, representing over 120 million unique patients. Since 2002 Vector One® has captured information on over 8 billion prescriptions representing over 200 million unique patients.

SDI Physician Drug & Diagnosis Audit (PDDA) with Pain Panel

SDI's Physician Drug & Diagnosis Audit (PDDA) with Pain Panel is a monthly survey designed to provide descriptive information on the patterns and treatment of diseases encountered in office-based physician practices in the U.S. The survey consists of data collected from over 3,200 office-based physicians representing 30 specialties across the United States that report on all patient activity during one typical workday per month. These data may include profiles and trends of diagnoses, patients, drug products mentioned during the office visit and treatment patterns. The Pain Panel supplement surveys over 115 pain specialists physicians each month. With the inclusion of visits to pain specialists, this will allow additional insight into the pain market. The data are then projected nationally by physician specialty and region to reflect national prescribing patterns.

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/s/

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drug use data cleared